The results of this study show (*a*) that a dose taken through the mouth is absorbed into the system giving the same type of elimination as a dose given intraperitoneally into the system of the rabbit, and (*b*) the expulsion of the overdose is almost identical with that exhibited in the case of the rabbit.

Conclusions. The authors of this paper as a result of the present investigations conclude that:

1. Germanium dioxide has a decided erythropoietic action in the guinea-pig, rabbit, dog and man.
2. This erythropoietic action exerts a certain periodicity as shown in all of the erythrocyte curves obtained.
3. Relatively large doses of germanium dioxide are distinctly toxic, and from the results obtained it can be roughly calculated that the lethal dose is about 586 mg. of germanium dioxide per kilo of body weight.
4. This toxic action is not explainable on the basis of the accumulation of the compound in the system but is possibly due to an overstimulation of the blood-forming organs.
5. The quantitative method as devised by the authors for the determination of germanium dioxide in animal tissues and excreta, both in the presence and absence of arsenic, is an accurate method.
6. Germanium dioxide does not accumulate but is eliminated through the kidneys and alimentary tract. The overdose being rapidly eliminated and occurring chiefly through the agency of the kidneys, elimination by way of the alimentary tract is small.

The authors wish to express their appreciation of the kindnesses extended to them by Drs. A. C. Abbott, D. H. Bergey and H. F. Smyth during the course of this work, and to thank them also for the many valuable suggestions received.

LATENT NEUROSYPHILIS IN EIGHT PER CENT OF MEDICAL PATIENTS IGNORED OWING TO NEGLECT OF LUMBAR PUNCTURE.

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How impossible it is for any group of specialists to "annex syphilology as a perquisite" has recently been remarked by a specialist in this field—Stokes, in 1920. An internist may therefore be permitted to oppose those who even today talk of "syphilomania" (Gandolfo in 1919) and "Wassermania" (De Meritt in 1920). The latter, for example, expresses the views of not a few "practical men" when he says, "I use this rather slangy term, the best I can invent, for a new and hitherto unamed psychosis. . . . the delusion that the health, the happiness and in fact the whole existence of syphilitic patients hang entirely on the results of frequent Wassermann tests."

Opposed to the above reactionary view we may group the demands for greater diffusion of our knowledge of syphilis, such as those by Cortlett in 1914, Collins in 1915, Irvine in 1916, White in 1917, Hazen in 1917, and most graphically perhaps by Pautrier in 1918, who wrote: "The ignorance of 95 per cent of doctors in dermato-venereology exceeds imagination. . . . It is truly scandalous. . . . The responsibility may be traced to a fearful gap in our medical teaching." This is startling testimony from a member of that nation which is currently believed to be particularly well-informed on this subject, a nation which has produced Alfred Fournier and his son Edmond Fournier. The former has more than once been called the first syphilographer of his time, and probably of all time; while with his son he is said, even by Dr. Leon Daudet in his extraordinary book of caustic comment on the best-known names in French medicine since 1880, to "have given to humanity out of an experience of forty years solutions to three-quarters of the problems of humanity."

Pleas, too, for more careful search in syphilitics for involvement of the cerebrospinal axis are nothing new. This is particularly true of lumbar puncture, but at the same time considerable conservatism is conspicuous in the recommendations as to the frequency with which it should be employed. These views progressively require puncture:

1. Only in proved syphilitics with frank neurological signs.
2. In patients with no nerve signs, but with mental symptoms.
3. In patients with neither nerve signs nor symptoms but only a suggestive history, such as of ptosis.
4. As a routine on every person known to have become infected with syphilis even though he has never shown symptoms.
5. The most advanced view of puncturing, despite denial of infection and despite a negative blood Wassermann, any individual reporting suggestive ills in a spouse, miscarriages, headaches, transitory lid-drop or any other unexplained nervous or mental symptoms.

The earliest downright demand for invariable lumbar puncture, and the one which stimulated the observations here reported, was that by Solomon in 1916. He agreed with Craig in 1915 in considering a positive Wassermann reaction as a symptom of syphilis; and recently, in 1920, in a most interesting paper, he gave further evidence of the reliability of the Wassermann reaction in competent hands, as illustrated by the remarkably parallel results reported on duplicates sent to the Boston City Department of Health (Dr. P. Castleman, director) and the Massachusetts State Department of Health (Dr. W. A. Hinton, director). From these standpoints he went on to maintain the thesis that: "Syphilis may be considered a disease of remissions and exacerbations, the latent period merely a remission, following which a severe lesion is to be expected. Therefore when we treat a patient having a positive Wassermann reaction during the period of latency we are not treating the reaction but rather the patient for the purpose of curing him of a chronic disease and thus preventing a flare-up." From this he went on to contend that "in every case showing a positive Wassermann reaction a lumbar puncture is indicated for the purpose of examining the spinal fluid." Together with the late Professor Southard he returned to the charge in 1917, asserting that evidence is seldom searched for until neuropsychiatric symptoms or signs have appeared, and even then is regrettably rarely recognized.

Personal Experience. This advanced attitude stimulated a desire to detect neglected syphilis, and especially neurosyphilis, in such general medical patients as passed through our hands at the U. S. Army Base Hospital 76 at Vichy, Allier, France. The necessary intensive examination could, owing to lack of time, be applied to only a limited number of patients—namely, those on a special nephritic ward. During the first month, November, 1918, there were admitted to this ward thirty-one renal cases. The kidney conditions in these men have been reported elsewhere. Not one had a syphilitic register or clinical signs strikingly syphilitic. With the incidental constant desire to exclude syphilis, however, Wassermann reactions were done on the blood of each patient and positive diagnosis then was made in four men, *i. e.*, 13 per cent; and in three of these lumbar puncture gave evidence of involvement of the central nervous system, namely, in 75 per cent of the syphilitics or in 10 per cent of the medical cases. Simultaneously, among the same number of consecutive patients in the adjoining ward, under treatment for bronchitis or so-called "influenza," again all without known syphilis, the disease was detected in four (history of chancre, strongly positive Wassermann reaction, and in 1 case a tertiary skin blotch at the elbow), and of these 2 had negative spinal fluids and 2 had pleolymphocytosis, with strongly positive Wassermann reaction on the fluid. Protocols of the latter four patients are not at hand, but for the first four mentioned are abridged below, omitting the tests relating to the cardiorenal system, which were reported in the previous article.

In sum, then, among 62 patients with medical complaints not pointing to syphilis were 8 cases with that disease unrecognized, *i. e.*, 13 per cent of the total; and in 5 among these 8 (*i. e.*, 63 per cent of the syphilitics) the organ most gravely affected was the central nervous system. These figures while striking are not statistically significant, owing to the small number of patients. They agree, however, with those reported by others. First, relating to the frequency of unsuspected syphilis among miscellaneous medical cases not previously supposed to be infected, but detected by routine Wassermann reaction, my 13 per cent falls between the 12 per cent reported by Walker and Haller in 1916 and the 17 per cent found by McLester in 1918. In the second place, as to the frequency of latent neurosyphilis in patients with positive bloods but hitherto supposedly normal central nervous system, Walker and Haller got 59 per cent, Corbus in 1917 got 30 per cent, Stokes and Brehmer in 1920 got 64 per cent, against the 63 per cent here reported.

Diagnosis of neurosyphilis was made after consideration of (*a*) the history, (*b*) the physical examination of the pupillary and patellar reflexes, coördination of finger-to-finger motions and of station (Romberg), (*c*) cells and complement-fixation in the spinal fluid. Such of these observations as were remarkable are recited in the protocols, and, as will there be seen, positive clinical findings were scarce, justifying, we believe, the consideration of these cases as belonging to the large group variously called unsuspected, cryptic, latent, ignored, asymptomatic, monosymptomatic or oligosymptomatic syphilis. The positive findings may be summarized. The history in the 4 case reports showed that 2 of the men (Rh. and Co.) had had treatment prior to service but none in the army, and that 2 (Le. and Rh.) had suggestive mental symptoms. Physical examination showed no skin or mucous membrane lesions; no general glandular enlargement; no heart or aortic disease; no eye-ground changes; no pathognomonic reflexes (especially note the normal pupils in patient Le.), though some slight abnormalities.

Apprehensions and Answers. Some may hesitate because of the possibility that the release of the cerebrospinal fluid may increase the permeability of the meninges for organisms circulating in the blood, as discussed for acute meningitides by Netter in 1887, 1909, 1911, 1915, Sicard in 1900, Achard and Laubry in 1902, Voisin in 1903, 1904, Sladen in 1910, Hutinel in 1912, Herrick in 1918, Weed, Wegeforth, Ayer and Felton in 1919, and especially exhaustively by Wegeforth and Latham in 1919. In answer it may be said: (*a*) That those observations related to acute meningococcus or pneumococcus septicemias, which are ordinarily excluded in chronic syphilis by the absence of fever and of other signs; (*b*) that so far little evidence is available to indicate that in syphilis the same process is to be feared; and (*c*) that even if such permeation to the spinal fluid be feared one can act safely by postponing lumbar puncture until the blood has been sterilized by intravenous injections of arsphenamin.

To those who hesitate because of the fear of causing headache, one may point out that this is practically always preventable by lying flat in bed for forty-eight hours, thus allowing the hole in the dura a chance to heal and stop the "occult leakage" and consequent lack of support to the brain, which was surmised to be the cause by Sicard, as cited by Widal in 1901 and confirmed by MacRobert in 1918 and by Wegeforth and Latham in 1919.

To those who hesitate because of the evidence that the cerebrospinal fluid may be abnormal only transiently, one may point out the words of Collins in 1920 on "Syphilitic Scars of the Spirit:" "The chief object in calling attention to this variety of cerebral syphilis is to emphasize the fact that although the infection is thwarted and the patient regains what seems to be his health, he is left with a scar of his mind. . . . The lesson is that the earlier the treatment is instituted the greater the chance of functional recovery."

Position of the Patient for Lumbar Puncture. On the suggestion of Dr. A. B. Brower, of Dayton, Ohio, the Sam Browne belt with sling removed was used instead of the knotted sheet placed by some around the neck to hold the chin against the knees, to keep the lumbar spine well arched and immobile and to afford the patient something firm to strain against. Out of twenty punctures only one patient made a "fuss" at the idea of the harness, and he finally consented to put it on himself. A plank was put under the mattress along the edge of the bed to prevent sagging and consequent lordosis of the patient, who lay on his left side. Besides this method of securing the good position so advantageous for insertion of the needle through muscular backs, morphin, 0.015 gm. s.c., was also administered to many of the patients.

Protocols. CASE III.—Gr., aged thirty-three years; laborer; private of infantry; service of ten months; measles in 1890; typhoid in 1909; venereal disease denied by name and symptoms, including rash, sore mouth and other secondaries, but exposures from 1902 to 1918.

Present Illness. Nocturia since October 26, 1918; dyspnea since October 26 on exertion only; edema of feet and face, marked from October 26 to November 8, only slight since; seen November 12, 1918 to January 11, 1919.

Examination. Reflexes: Pupils equal; irregular; react poorly; KJ normal; Romberg normal; serum Wassermann reaction strongly positive; cerebrospinal fluid cells 0; Wassermann reaction negative.

Diagnosis: (1) Syphilis; (2) nephritis, acute, October 26, due to exposure, severe; (3) hypertension.

After-history: Follow-up letter in March, 1921, not answered.

CASE X.—Le., aged thirty-two years; piano teacher; private of engineers; service of seventeen months; venereal exposure denied but probably acquired from wife; married in June, 1917, separated in three months because she gadded about and went often to a doctor, but would not tell why (*cf.* case reported by Gooken in 1919).

Present Illness. Headache since fall of 1917, (?) due to syphilitic meningitis; sensitive to cold since May, 1918; loss of memory since July 20, 1918; previously played concertos from memory; nocturia since September 20, 1918; dyspnea since October 3, 1918; (?) due to syphilitic myocarditis; November 1, 1918, mental concentration impaired; November 9, incontinence.

Physical Examination. Eyelids puffy; pupils equal; circular and react well to light; KJ equal but hyperactive; no Romberg; no hand ataxia; hyperactive rectus and cremasteric reflexes; the only palpable glands are two in the left axilla. Serum Wassermann reaction strongly positive; cerebrospinal fluid and Wassermann reaction strongly positive, cells 46. Seen from November 19, 1918, to January 19, 1919.

Diagnosis: (1) Neurosyphilis; (2) nephritis, acute; onset September 20, 1918, due to exposure or possibly to syphilis, apparently in early stage of nephritis.

After-history: Letter in March, 1921, not answered.

CASE XXVI.—Rh., aged twenty-nine years; pay-roll clerk; private in field artillery; service fourteen and a half months; measles at six; mumps at seven; typhoid in 1912; gonococcus urethritis in 1916, treated for one month; also in 1916 both soft and hard chancres treated with injections into the paravertebral muscles of six ampules of (?); no mercury iodide or arsenic so far as he knows; no secondaries. Scabies for two months in 1916 and from October 1 to December 31, 1918. Concussion by burial up to the waist in a collapsed dug-out October 10, 1918; mild; cured October 10; sprain of right knee by that burial; cured October 26; abrasion of the right knee from falling timber in same dug-out October 8; cured November 18; influenza November 20 to 25, 1918; exposure to weather for the past two months; habits, alcohol in excess.

Present Illness. Nocturia since November, 1917; sleep restless since July 1918, *i. e.*, for five months; "lightheaded" in October and November, 1918; numbness in the lower legs for a month; no lancinating pains or crises.

Examination. Pupils equal but irregular and react poorly, KJ normal; Ach. J. equal but hyperactive. Romberg: slight; hand ataxia slight; serum Wassermann reaction strongly positive; cerebrospinal fluid Wassermann reaction strongly positive; cells 210. Seen December 5, 1918, to January 19, 1919.

Diagnosis: (1) Neurosyphilis, onset 1916; (2) nephritis, chronic, onset in November, 1917, apparently due to exposure.

After-history: Letter in March, 1921, not answered.

CASE XXXI.—Co., aged twenty-seven years; carpenter; private of infantry; service five and a half months; diphtheria; mumps and scarlet fever at about three; chicken-pox, measles and pneumonia at four years; scabies in 1904, typhoid in 1908, chancre in 1911, treated by 75 pills (? Hg), no KI or 606. Gonococcus urethritis in 1917 for three weeks; diarrhea September 6 to December 4, 1918;

exposure to weather for the last two months; eats considerably more meat and salt than the average.

Present Illness. G. S. W. right thigh. Seen December 10, 1918, to January 19, 1919.

Examination. Pupils equal, irregular and react poorly; KJ equal but rather hyperactive; Romberg slight. Glands: ax. and ing. slight; spleen 3 cm. below C.M., serum Wassermann reaction strongly positive, and cerebrospinal fluid Wassermann reaction strongly positive; cells 25.

Diagnosis. (1) Syphilis, onset 1911; (2) neurosyphilis, onset ?; (3) splenomegaly, onset ?; (4) nephritis, acute, onset December, 1918, apparently due to diarrheal infection.

After-history: In March, 1921, wife reports patient dead, cause unknown.

Summary. 1. In 62 medical cases, all supposedly non-venereal, were found 8 syphilitics, only 2 of whom knew of their disease.

2. In these 8 syphilitics were 5 with C. N. S. involvement, hitherto unrecognized in all.

3. The army principle of relying on the physical examination and neglecting the history leads to the overlooking of syphilis in the army.

4. Since neurosyphilis is so important it should be more generally suspected in an internal medical clinic.

5. Lumbar puncture should be done (preferably after preliminary fundus examination) on every syphilitic. If positive it should be repeated rather frequently, at least annually, until it has been negative for one year; and thereafter every two years, to exclude recurrence. This, though drastic, is milder than tabes or G. P. I. Watchful waiting in syphilis does far more harm than occasional accidents incident to puncture.

6. The Sam Browne belt was a useful adjunct.

I am indebted to former associates in Base Hospital 76, especially Dr. I. I. Lemann; of New Orleans, Dr. A. B. Brower, of Dayton, Ohio, and Mr. E. E. Wagner, of Newport News.

BIBLIOGRAPHY.

References are given only to some of the more pertinent papers. In these the other authors cited may be found, or else in the *Index Medicus*. Since this paper was submitted in May, 1921, the literature has shown a number of articles on the importance of the early diagnosis of neurosyphilis.

1. Achard and Laubry: Gaz. hebd. de méd., April, 1902.
2. Collins, J.: Jour. Am. Med. Assn., May 1, 1920, 74, 1216.
3. Corlett, W. T.: Jour. Cutan. Dis., February, 1914, 32, 117.
4. Corbus, B. C.: Jour. Am. Med. Assn., December 22, 1917, 69, 2087.
5. Craig, C. F.: Am. Jour. Med. Sc., January, 1915, 149, 41.
6. Daudet, L.: Devant la douleur, Souvenirs des milieux médicaux, Paris, 1915.
7. DeMeritt, C. L.: Jour. Med. Soc. of New Jersey, March, 1920, 17, 89.
8. Gray, H.: Jour. Urol., December, 1919, 3, 459.

9. Gray, H.: Arch. Neurol. and Psych., July, 1921, 6, 61. This paper reviews thoroughly the literature on lumbar puncture in relation to syphilis.
10. Hazen, H. H.: Am. Jour. Syph., January, 1917, 1, 135.
11. Herrick, W. W.: Arch. Int. Med., 1918, 21, 541.
12. Hutinel: Maladies des Meninges, Paris, 1912.
13. Irvine, H. G.: Jour. Am. Med. Assn., 1916, 67, 1987.
14. MacRobert, R. G.: Jour. Am. Med. Assn., May 11, 1918, 70, 1350.
15. McLester, J. S.: Am. Jour. Med. Sc., March, 1918, 155, 320.
16. Netter, A.: Bull. de l'acad. de méd., Paris, 1909, 62, 106.
17. Pautrier, L.: Jour. med. français, December, 1918, 8, 213.
18. Sicard, J. A.: Les injections sous-arachnoidiennes, Thèse, Paris, 1900.
19. Sladen, F. J.: Johns Hopkins Hosp. Rep., 1910, 15, 397.
20. Solomon, H. C.: Jour. Am. Med. Assn., March, 1920, 74, 788.
21. Solomon, H. C.: Interstate Med. Jour., August, 1916, 23, 643.
22. Southard, E. E., and Solomon, H. C.: Neurosyphilis, Boston, 1917.
23. Stokes, J. H.: Arch. Derm. and Syph., October, 1920, n.s., 2, 473.
24. Stokes, J. H., and Brehmer, H. E.: Jour. Indust. Hyg., January, 1920, 1, 419.
25. Voisin, R.: Thèse, Paris, 1904.
26. Voisin, R., and Laignel-Levastine: Arch. de méd. expér., 1903, p. 207.
27. Walker, I. C., and Haller, D. A.: Jour. Am. Med. Assn., February 12, 1916, 66, 483.
28. Weed, L. H., Wegeforth, P., Ayer, J. B., and Felton, L. D.: Jour. Am. Med. Assn., January 18, 1919, 72, 190.
29. Wegeforth, P., and Latham, J. R.: Am. Jour. Med. Sc., August, 1919, 158, 183.
30. White, C. J.: Am. Jour. Syph., 1917, 1, 144.

ROENTGEN-RAY STIMULATION OF THE PANCREAS IN EXPERIMENTAL PANCREATIC DEFICIENCY.

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and

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In a preliminary communication[1] we have called attention to the fact that with roentgen stimulation of organs two distinct methods of approach may be considered, the one direct and the other indirect. The first would include the stimulation of dys- or hypofunctioning organs with the purpose of restoring function to the normal plane. The treatment of anuria in acute parenchymatous nephritis; hepatic intoxication in some forms of cirrhosis; achylia; anemia of certain types; particularly endocrine disturbances—the ovaries in some forms of amenorrhea, the testicles (as in Steinach experiments), the hypophysis in growth disturbances, the adrenals in Addison's disease, the pancreas in diabetes—are but a few illustrations of the possibilities of this first method.

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[1] Petersen, W. F., and Saelhof, C. C.: Jour. Am. Med. Assn., 1921, 76, 718.